

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
6 January 2005 (06.01.2005)

PCT

(10) International Publication Number  
**WO 2005/000197 A3**

(51) International Patent Classification<sup>7</sup>: **C07D 487/04**

(21) International Application Number:  
PCT/US2004/011297

(22) International Filing Date: 12 April 2004 (12.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/462,554 11 April 2003 (11.04.2003) US

(71) Applicant (for all designated States except US): **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; Office of Technology Management, 185 Berry Street, Suite 4603, San Francisco, CA 94107 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **TAUNTON, Jack** [US/US]; 2920-22nd Street, San Francisco, CA 94110 (US). **COHEN, Michael** [US/US]; 166 Locksley Avenue, Apt. 1, San Francisco, CA 94122 (US). **SHOKAT, Kevan** [US/US]; 783-35th Avenue, San Francisco, CA 94121 (US). **ZHANG, Chao** [CN/US]; 1515-27th Avenue, San Francisco, CA 94122 (US).

(74) Agents: **ACKERMAN, Joel, G. et al.**; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111-3834 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
1 September 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **SELECTIVE SERINE/THREONINE KINASE INHIBITORS**

(57) Abstract: Inhibition of protein kinases having one or more cysteine residues within the ATP binding site is effected by contacting the kinase, per se or in a cell or subject, with an inhibitory-effective amount of a compound having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of reacting with a cysteine residue within the ATP binding site of a kinase. Preferred compounds include certain pyrrolopyrimidines and oxindoles having such an electrophilic substituent and optionally an aromatic or heteroaromatic substituent that is capable of interacting with a threonine or smaller residue located in the gatekeeper position of the kinase. Kinases lacking such cysteine residues may be engineered or modified so that they are capable of being inhibited by such compounds by replacing a valine or other amino acid residue within the ATP binding site by a cysteine residue.

WO 2005/000197 A3

this page blank (uspto)

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/11297

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07D 487/04

US CL : 544/280; 514/265.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 544/280; 514/265.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAS ONLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BURCHAT, A.F. et al. Pyrrolo[2,3-d]pyrimidines Containing an Extended 5-Substituent as Potent and Selective Inhibitors of Ick II, Bioorganic & Medicinal Chemistry Letters. 02 October 2000, Vol. 10, No. 19, pages 2171-2174, see compounds 5, 10, and 11, page 2172 fit formula (I) with R1 = NH2, R2 = 4-methoxyphenyl, R3 = E = CN, CO2H, or CONH2, R4 = cyclopentyl, and R5 = H.	1-4 and 6-11
X	CHENON, M.T. et al. Carbon-13 magnetic resonance. XXV. Basic set of parameters for the investigation of tautomerism in purines established from carbon-13 magnetic resonance studies using certain purines and pyrrolo[2,3-d]pyrimidines. Journal of the American Chemical Society. 1975, Vol. 97 No. 16, pages 4627-36, especially compound IV, page 4628 fits formula (I) with R1 = NH2, R2 = R3 = E = R5 = H, R4 = methyl..	1-3 and 5

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

11 June 2005 (11.06.2005)

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Date of mailing of the international search report

05 JUL 2005

Authorized officer

Thomas C. McKenzie, Ph.D.

Telephone No. (571) 272-1600

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/11297

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 18,19 and 61-63  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-17,20-25,48 and 49
- Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US04/11297

### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-17, 20-25, 48, and 49, drawn to pyrrolopyrimidine compounds and a method of use thereof.

Group II, claim(s) 26, and parts of 30-46, and 50, drawn to compounds of formula (II) and a method of use thereof.

Group III, 27, and parts of 30-46, and 50, drawn to compounds of formula (III) and a method of use thereof.

Group IV, 28, and parts of 30-46, and 50, drawn to compounds of formula (IV) and a method of use thereof.

Group V, 28, and parts of 30-46, and 50, drawn to compounds of formula (V) and a method of use thereof.

Group VI, claim(s) 47, drawn to a method of inhibiting protein kinases, using any compound.

Group VII, claim(s) 51, drawn to a second method of affecting protein kinases using any compound.

Group VIII, claim(s) 52, drawn to a third method of affecting protein kinases.

Group IX, claim(s) 53, drawn to a method of treating a cell with any compound.

Group X, claim(s) 54 and 59, drawn to a method of tumor treatment with any compound.

Group XI, claim(s) 55-57, drawn to a second method of use of pyrrolopyrimidine compounds.

Group XII, claim(s) part of 58, drawn to a second method of use of compounds (II).

Group XIII, claim(s) part of 58, drawn to a second method of use of compounds (III).

Group XIV, claim(s) part of 58, drawn to a second method of use of compounds (IV).

Group XV, claim(s) part of 58, drawn to a second method of use of compounds (V).

Group XVI, claim(s) 60, drawn to an array.

The inventions listed as Groups I-X and XVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the technical feature of claim 1 is a pyrrolopyrimidine compound. This technical feature is not present in claims 26-47, 50-54, and 59.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/11297

The inventions listed as Groups I and XI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Claims 48 and 49 are drawn to a method of use of the compounds of Group I. Claims 55-57 are drawn to a second method of use of these compounds. According to Appendix A1 ANNEX B PART 1(e)(i) of the ADMINISTRATIVE INSTRUCTIONS UNDER THE PCT, only a single use of a product shall be examined.

The inventions listed as Groups II-V and XII-XV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Claim 50 is drawn to a method of use of the compounds of Groups I-V. Claim 58 is drawn to a second method of use of these compounds. According to Appendix A1 ANNEX B PART 1(e)(i) of the ADMINISTRATIVE INSTRUCTIONS UNDER THE PCT, only a single use of a product shall be examined.